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Indirect community protection against influenza by vaccinating children: a review of two recent studies from Italy and the United States

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A secondary effect of influenza in childhood is the impact -medical, social and economic- on the family. Two recently published studies have considered how the vaccination of children against influenza may help control the spread of influenza through indirect protection of susceptible persons.

An Italian study [1] conducted prospective multicentre research into children with respiratory tract infections (RTI) to determine the burden of laboratory confirmed influenza in healthy children and their households. Altogether, 3771 otherwise healthy children aged <14 years and presenting to primary care centres and emergency departments with symptoms of RTI were followed up until the resolution of their illness; 352 (9.3%) were positive for influenza virus. Children with laboratory confirmed influenza were significantly more likely to present with fever ($p<0.0001$) and with croup ($p<0.0001$). They also had significantly longer mean school absence (5.10 days (standard deviation (SD) 2.55) versus 4.25 days (SD 2.93), $p<0.0001$), although the prevalence of hospitalisation was similar. The households of influenza positive children had significantly more respiratory tract infections (15.1% versus 9.5%, $p<0.0001$), medical outpatient visits ($p<0.0001$), lost work days ($p<0.0001$ for their own illness; and, $p<0.0001$ for their child's illness) and lost school days for siblings ($p<0.0001$).

The results of this study suggest that influenza is likely to be transmitted to household contacts and has a substantial household impact in terms of illness and lost school and work days. The authors conclude that these effects could be reduced by the vaccination of healthy children. However, there were no significant differences in hospitalisation rates between the groups, no information on the ages of other siblings that might determine both sibling and parental absence, or any mention of loss-to-follow up.

A study from the United States [2] performed a non-randomised community-based controlled trial in five communities to assess the benefit of vaccinating children with cold-adapted intranasal

influenza vaccine. Healthy children aged 18 months to 18 years in two of the communities were offered vaccine for three consecutive years. The analysis was restricted to members of a particular health plan, which, in the intervention towns, comprised approximately half of those vaccinated and covered approximately two thirds of the population, but covered only about 10% of the population in the comparison towns. Any differences between the health plan population and the rest of the population are not described. Age-specific rates of medically attended acute respiratory illnesses during the influenza outbreak period were calculated for both the intervention and control communities. Altogether, 20%-25% of eligible children in vaccination communities received vaccine each season, which was generally a good match to the circulating virus.

The authors reported a significant indirect protection in adults aged 35 years and over although percentage differences in illness rate between the intervention and control arms appeared quite small: 17.6 % compared with 18.6% in year 1, 17.1 versus 18.8% in year 2, and 15.1 versus 17.8% in year 3, giving a protective efficacy (1 minus relative risk) of 8% (95% confidence interval (CI) 4%, 13%), 18% (95% CI 14%, 22%) and 15% (95% CI 12%, 19%) in years 1-3 respectively. This small effect may be translated into quite a substantial absolute number of consultations when multiplied up for population size, but appeared to have little effect on herd immunity during the influenza epidemics. This may be partly explained by the low uptake of less than 25% and may be diluted by using clinical rather than laboratory endpoints. Studies with a higher uptake rate, a randomised design and larger numbers of communities are needed to define the levels of indirect protection that could be achieved.

The evidence for the protection of the community against influenza by vaccinating children is limited. There are several randomised controlled trials which address the protection of household or school contacts inadequately, usually as a lower order outcome measure for which the study is not designed [3-8] Until now, only one community intervention trial [9] and one large ecological 'natural experiment' in Japan that assessed the effects on the wider community of vaccinating school children, had been made [10]. Both are suggestive of population benefit, but not necessarily conclusive. The US study [2] had a similar design to the community intervention study [9], but examined a larger number of communities and had a more consistent system for identifying respiratory illness (although it also had incomplete follow-up). Unfortunately, vaccine coverage was only about one quarter of that in the earlier Japanese study.

There is considerable variation in influenza vaccination policy in Europe – a table showing the current recommendations is available on the European Influenza Surveillance Scheme website (http://www.eiss.org/html/vaccination.html). The most common policy is to target high-risk groups (such as the elderly). This, however, can never be fully successful, despite high coverage, as influenza vaccine has lower efficacy in these patients, particularly frail, elderly people. There is evidence that children play a major role in the transmission of influenza to vulnerable persons [11]. Therefore, a complementary strategy would be to provide indirect protection by vaccinating children, which would also have the benefit of direct protection to those vaccinated. Indeed, to reduce disease in children the US has recommended vaccination of all aged 6-23 months since 2003. Both of the studies reviewed suggest that indirect protection could be achieved in the community by the vaccination of healthy children. However, neither provides sufficient evidence to support this claim or to warrant the intervention at present, particularly at the levels of vaccine coverage observed.

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